

Claims

1. A method for qualitative or quantitative detection of a nucleic acid in a sample by means of amplification of this nucleic acid and by employing one or several detection probe(s) that bind reversibly to the amplifiable/amplified nucleic acid and, because of this property, enable a detection of the nucleic acid to be detected, characterized in that the method is carried out in the presence of a control nucleic acid in the sample that is also amplifiable, wherein the control nucleic acid binds the same detection probe(s) as the nucleic acid to be detected but has at least one deviation in the nucleotide sequence of the binding region for the probe(s) in comparison to the nucleic acid to be detected, such that the products of the nucleic acid to be detected and probe(s), on the one hand, and of the control nucleic acid and probe(s), on the other hand, have a different melting point, wherein the temperature difference of the melting points is sufficiently large in order to be able to analytically differentiate the two products from one another.
2. The method according to claim 1, characterized in that the melting point of the product of control nucleic acid and probe(s) is lower than that of the product of nucleic acid to be detected and probe(s).
3. The method according to claim 1 or 2, characterized in that the temperature difference of the melting points is at least 5 °C, preferably at least 10 °C, and even more preferred at least 15 °C.
4. The method according to one of the claims 1 to 3, characterized in that the control nucleic acid is amplified with the same primers as the nucleic acid to be detected.
5. The method according to one of the preceding claims, characterized in that the amplification of the nucleic acid is carried out by means of PCR.

6. The method according to one of the preceding claims, characterized in that two or more nucleic acids are detected in one and the same sample wherein the method is carried out in the presence of a control nucleic acid for each nucleic acid to be detected.

5 7. The method according to one of the preceding claims, characterized in that the nucleic acid to be detected is a DNA or an RNA derived in particular from a pathogen.

8. The method according to one of the preceding claims, characterized in that the presence of the nucleic acid in the sample is observed by means of real-time methods.

9. The method according to claim 8, characterized in that the detection of the nucleic acid is carried out at a temperature that is 2-10 °C below the melting temperature of the product of the nucleic acid to be detected and probe(s).

10. The method according to claim 9, characterized in that the product of control nucleic acid and probe(s) has such a low melting point that it is negligible or not at all present in the detection of the nucleic acid to be detected.

11. The method according to one of the preceding claims, characterized in that only one probe is used and the detection of the nucleic acid is realized by means of the melting curve of this nucleic acid in the presence of the probe wherein the melting curve of the control nucleic acid in the presence of this probe serves as an internal control for the correct course of the amplification.

12. The method according to one of the claims 1 to 10, characterized in that two detection probes are used for detection of the nucleic acid, wherein one of them carries a reporter group and the other changes the observable properties of the reporter group when it reaches a position in the vicinity of

the reporter group.

5 13. The method according to claim 12, characterized in that a detection probe is used for detecting the nucleic acid which detection probe carries a reporter group and a second group that changes the observable properties of the reporter group when it reaches a position in the vicinity of the reporter group, wherein the reporter group and the second group are positioned so close to one another such that the observable properties of the reporter group are changed either only during binding of the detection probe to the nucleic acid or only in the non-bonded state of the detection probe.

10 14. The method according to one of the preceding claims, characterize in that the nucleotide sequence of the control nucleic acid in the binding region for the detection probe(s) has at least two modifications relative to the nucleic acid to be detected, wherein preferably at least one of them is an exchange of a G or a C.

15 15. The method according to one of the preceding claims, characterized in that the sequence region of the control nucleic acid that can neither hybridize with a detection probe nor optionally with a primer is shortened.

20 16. The method according to one of the preceding claims, characterized in that the sequence of the control nucleic acid has significant deviations relative to the nucleic acid to be detected in the region that can neither hybridize with a detection probe nor optionally with a primer.

25 17. Use of a control nucleic acid in one of the methods according according to claims 1 to 16, characterized in that its nucleotide sequence in the binding region for the detection probe(s) has at least one modification relative to the nucleic acid to be detected.

18. Use of a control nucleic acid in one of the methods according to claims 1 to 16, characterized in that its nucleotide sequence in the binding region for the detection probe(s) has at least two, preferably three to five, modifications relative to the nucleic acid to be detected.

19. Use of a control nucleic acid in a method according to claims 1 to 16, characterized in that its sequence region that can neither hybridize with a detection probe nor optionally with a primer is shortened.

20. Use of a control nucleic acid in a method according to claim 1 to 16, characterized in that its sequence in that region that can neither hybridize with a detection probe nor optionally with a primer has significant deviations relative to the nucleic acid to be detected.

21. Use of a control nucleic acid according to claim 18, characterized in that the modifications are distributed approximately uniformly across the binding region for the detection probe(s).

22. Kit, comprising a nucleic acid that is suitable particularly as a control nucleic acid for the negative control in a method for detecting a nucleic acid to be detected, as well as a probe system with one or several oligonucleotide-containing probes, whose probe(s) can bind to the control nucleic acid and which has a reporter group with an observable property that changes as a function of whether the probe(s) of the system is/are bonded or not to said nucleic acid, characterized in that the nucleic acid that is particularly suitable as a controlled nucleic acid in at least one of the regions in which the oligonucleotides of the probe(s) of the probe system can bind, has at least one mismatch relative to the oligonucleotide of the probe(s) binding in said region.

23. Kit according to claim 22, wherein the nucleic acid particularly suitable as a

control nucleic acid has at least 2, preferably three to 5, mismatches.

24. Kit according to one of the claims 22 or 23, wherein the mismatches of the nucleic acid particularly suitable as a control nucleic acid is essentially uniformly distributed across the binding region for the oligonucleotide of the probe(s).